FIG. 1

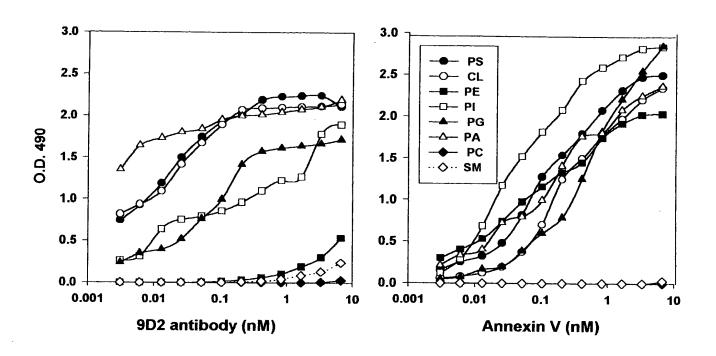


FIG. 2A

FIG. 2B

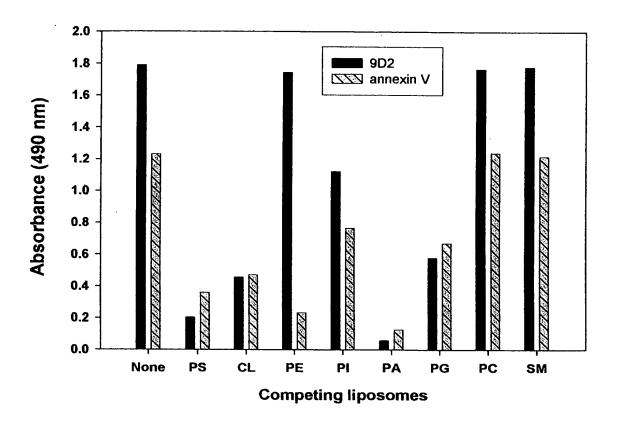


FIG. 3

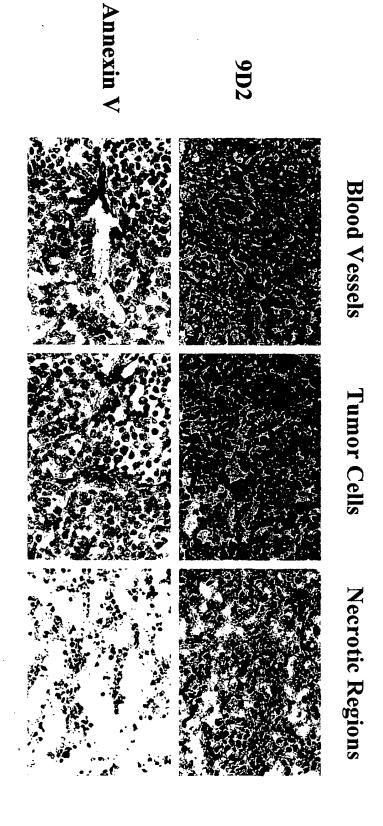


FIG. 4

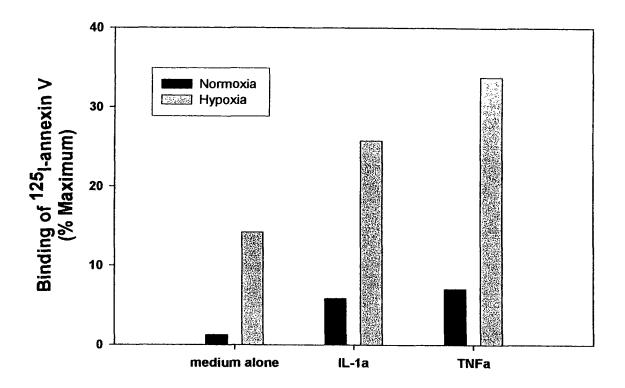
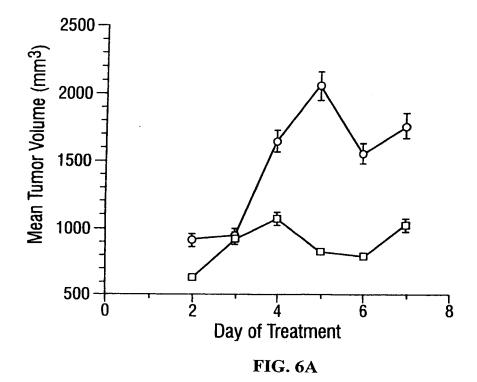
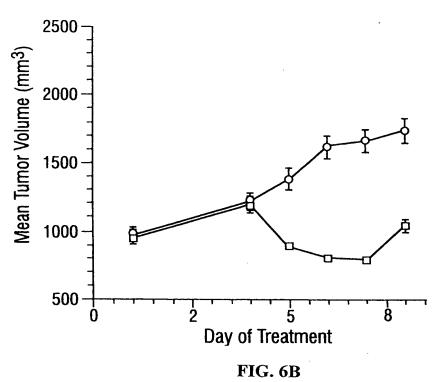


FIG. 5





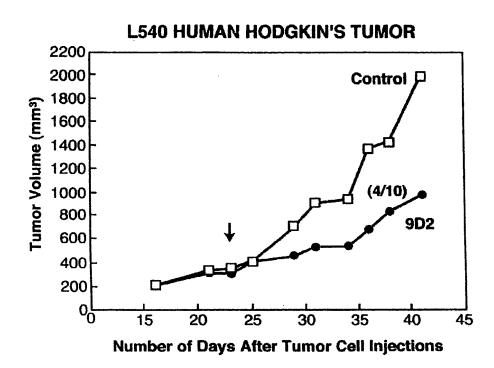
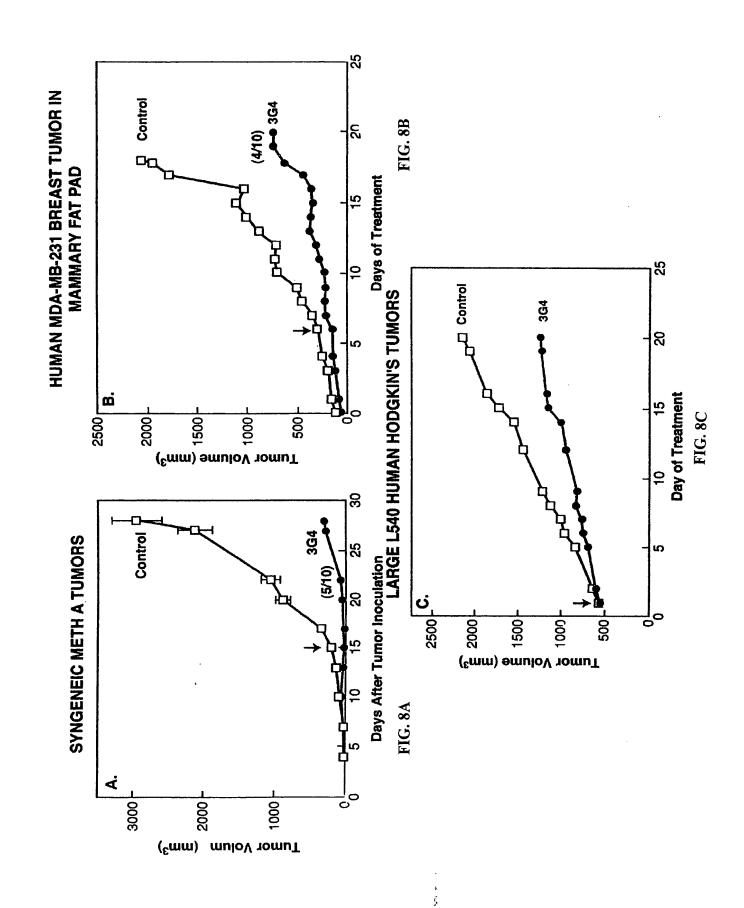
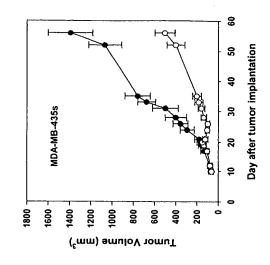
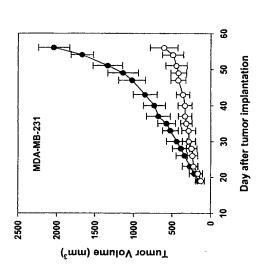


FIG. 7







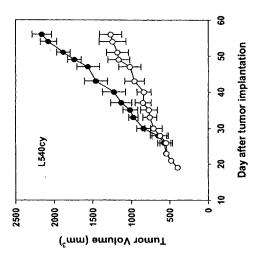


FIG. 8F

FIG. 8E

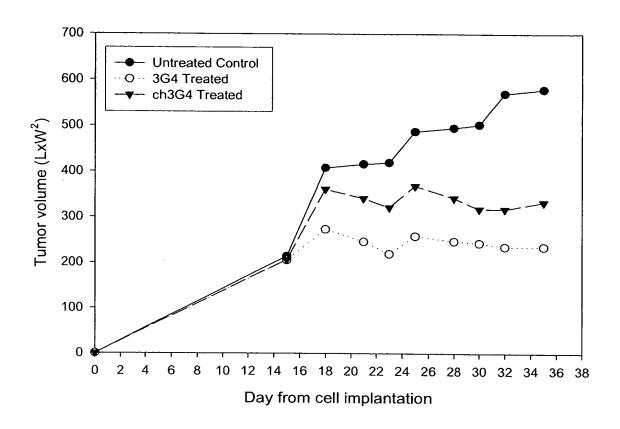
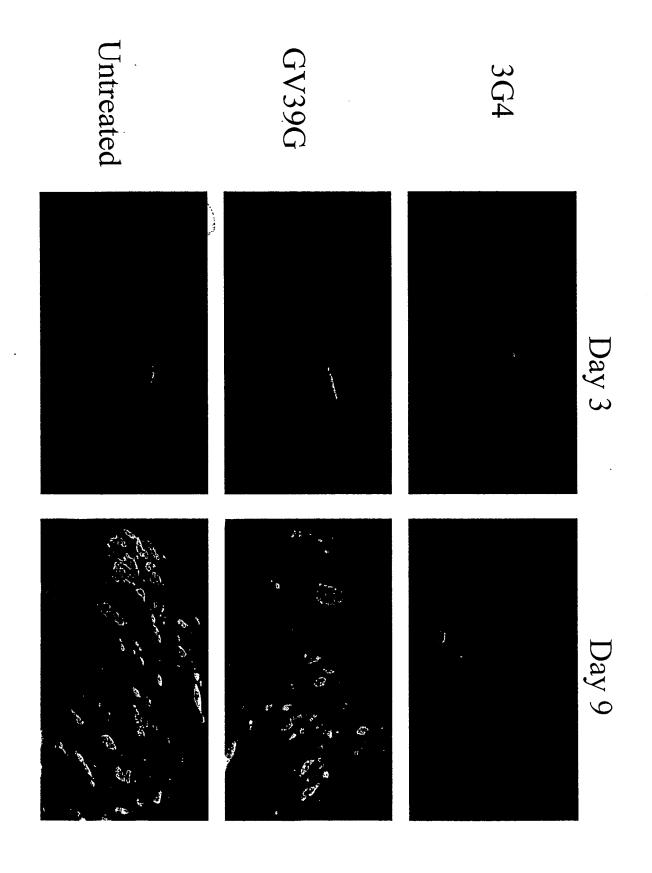
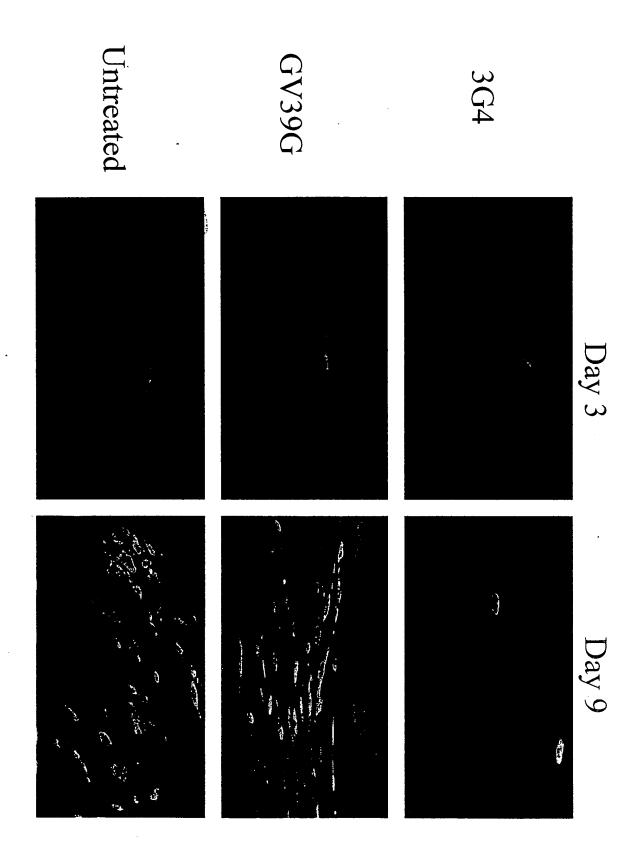


FIG. 8G

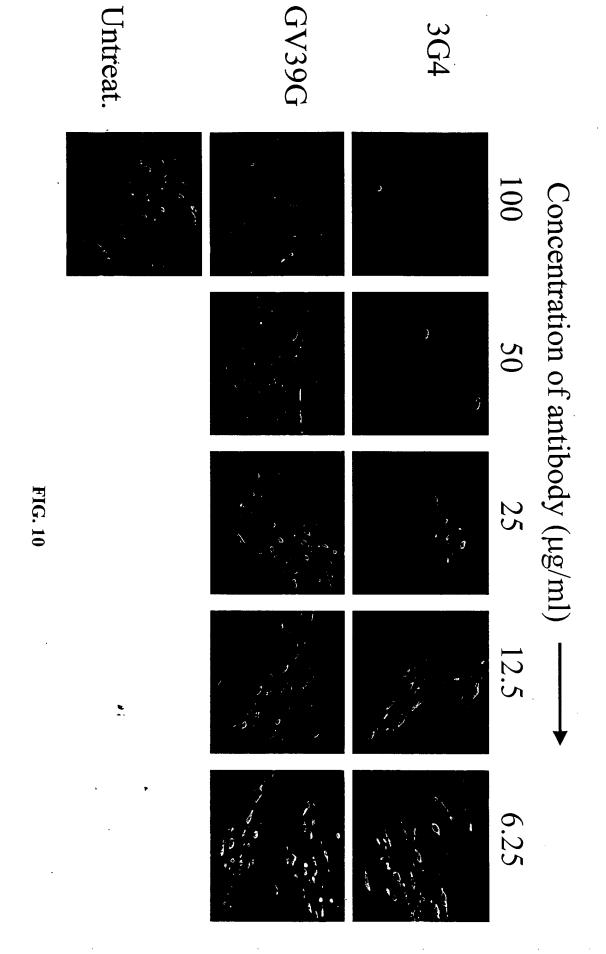


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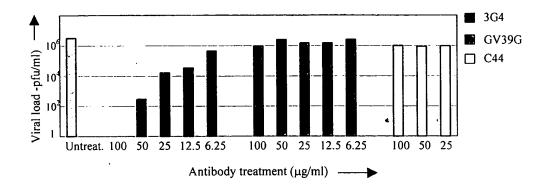


FIG. 11A

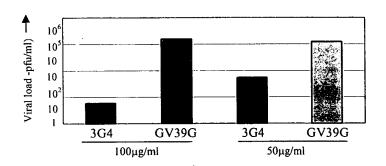


FIG. 11B

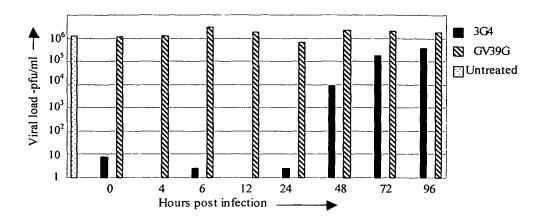


FIG. 11C

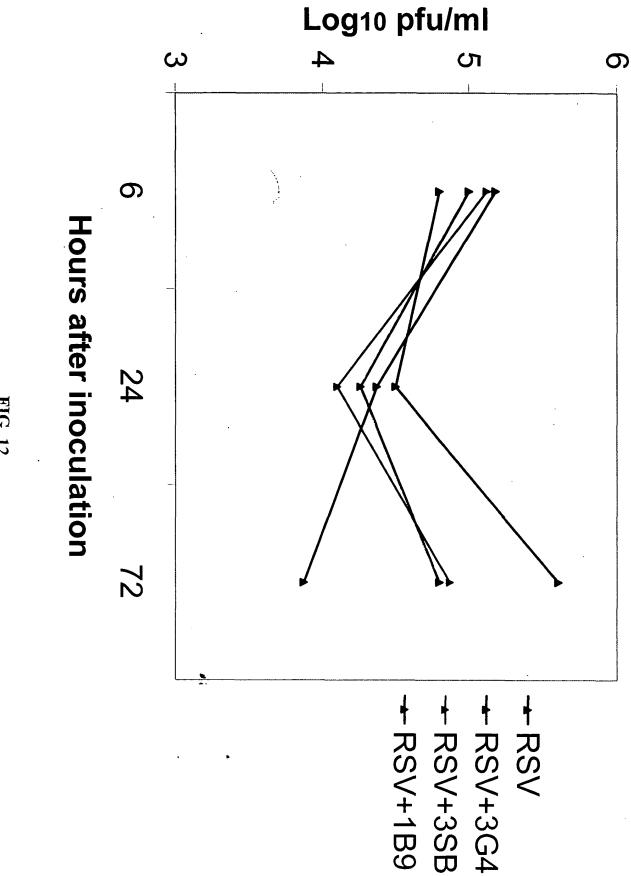


FIG. 13A. DLB

Duramycin — NH. CO. (CH₂)₅. NH. CO — biotin

+ NH₂. CI

Duramycin —

FIG. 13B. DIB

- NH. C. (CH₂)₃. S. CH₂. CO. NH. (CH₂)₆. NH. CO -- biotin

NA = neutravidinB = biotinDur = Duramycin Dur ww(B) NA FIG. 13C. (DLB)₄NA

n = 5 to 8 Duramycin residues per IgG Monomer (150,000 Da) is shown

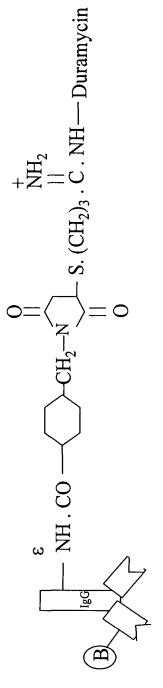
FIG. 13F. (DIM), HIgG-F

n = 5 to 8 Duramycin residues per IgG

(F) = fluorescein

Monomer (150,000 Da) is shown

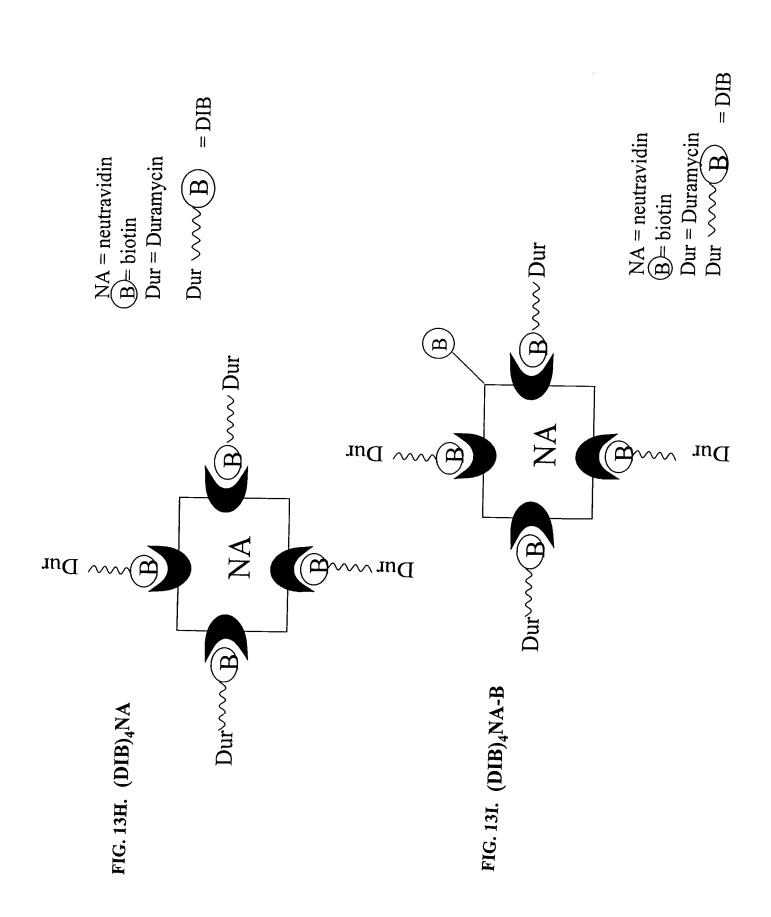
FIG. 13G. (DIM)_n HIgG-B



n = 5 to 8 Duramycin residues per IgG

(B) = biotin

Monomer (150,000 Da) is shown



Duramycin — NH_2 . CH_2 . CH_2 . SO_3

Duramycin — NH. C. CH_2 . CH_2 . CH_2 .

FIG. 13K. DS-2

 SO_3

Duramycin — NH . C

FIG. 13M. DS-4

$$\begin{array}{c} \overset{+}{\operatorname{hH}_2}. \, C\overline{I} \\ | \\ | \\ | \\ Dur - \operatorname{NH}. \, C. \, CH_2. \, CH_2. - S \xrightarrow{\hspace{1cm} \bigcap \\ \hspace{1cm} | \\ \hspace{1cm} | \\ \end{array}} N - CH_2 \xrightarrow{\hspace{1cm} \bigcap \\ \hspace{1cm} | \\ \hspace$$

 SO_{3}

FIG. 13N. DS-5

+ Duramycin — NH₂. CH₂. CH₂. CH₂. CH₂. SO3

+ NH,

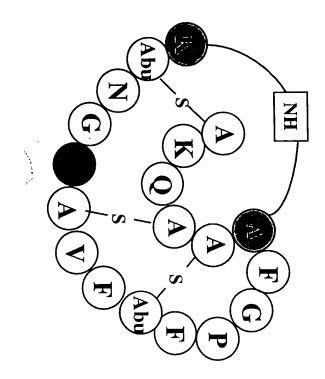
NH₂. Cl

Duramycin — NH.C.CH2.CH2.CH2.SS—

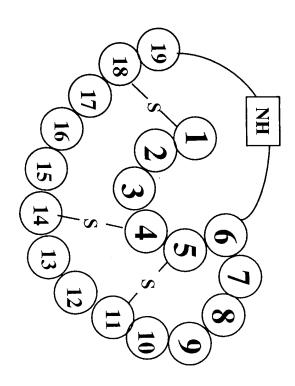
 $-NO_2$

_000×

FIG. 130. DC-1







Lanthionine Ala-S-Ala

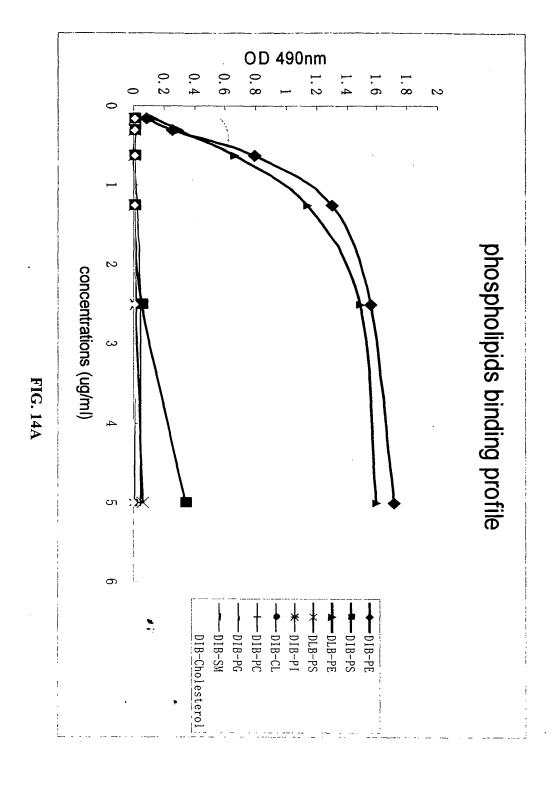
NH₂

cystine

β-methyllanthionine Abu-S-Ala

Lysinoalanine Ala-NH-Lys

R= OH, as in cidofovir, or labile hydrophobic group



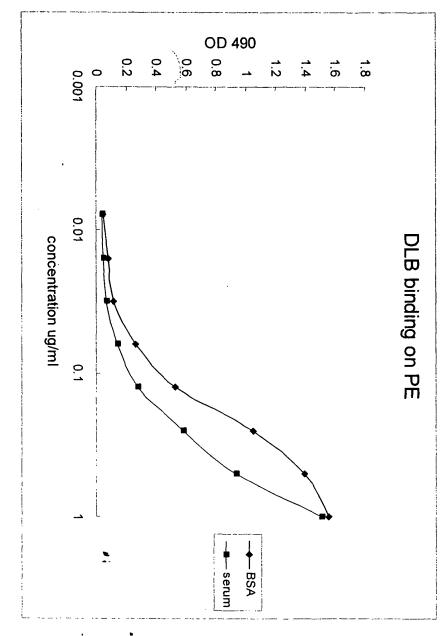
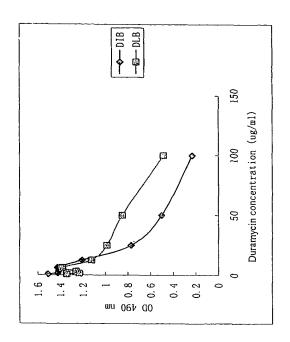


FIG. 14B



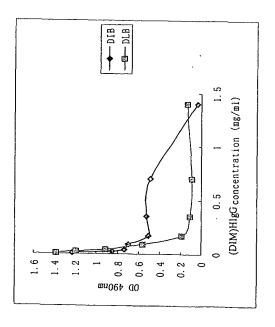


FIG. 14D

FIG. 14C

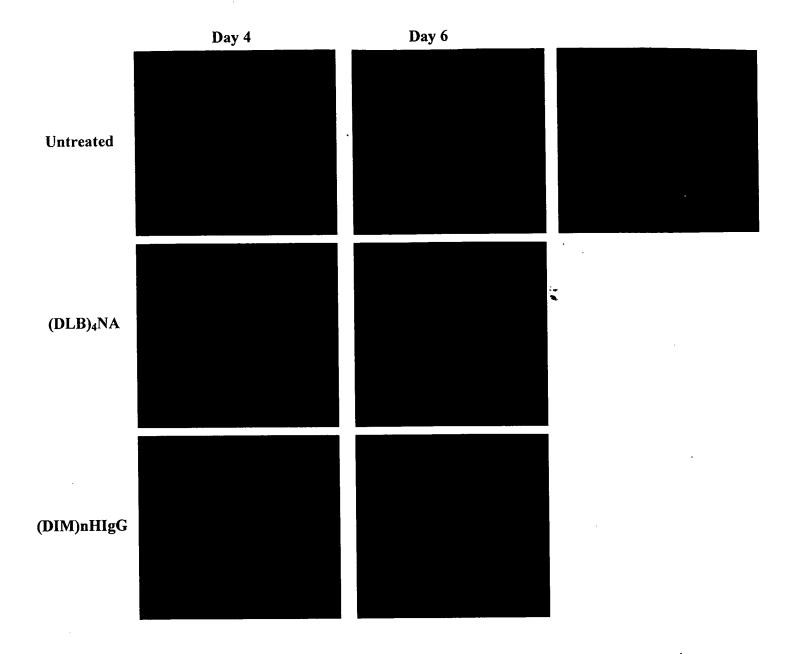
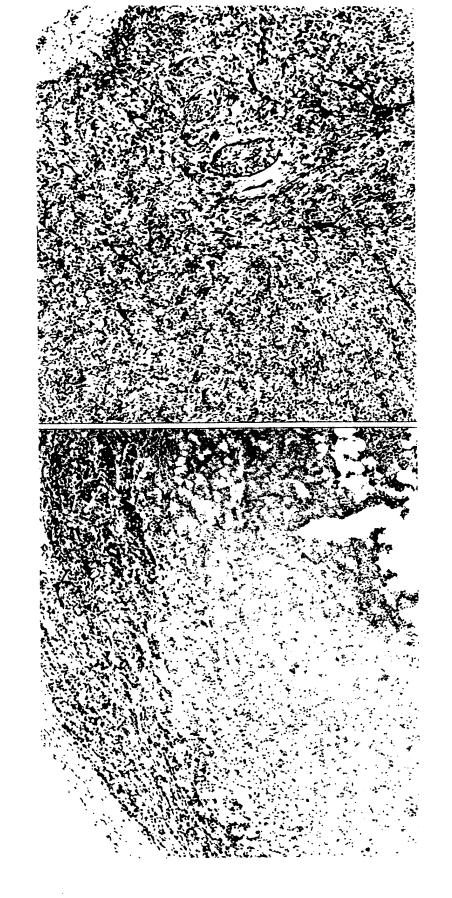
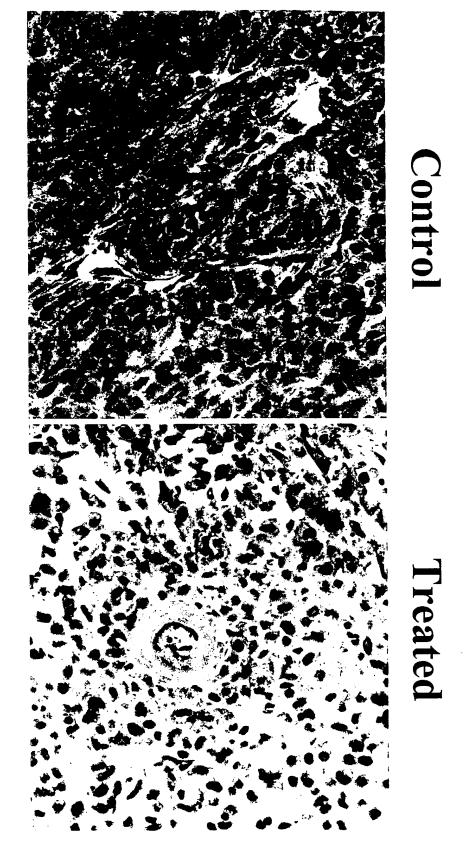


FIG. 15



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FIG. 18A

3G4-2BVH original sequence:

121																			S TCA AGT	
									Pvu	ΙI										
									~~~	~~~	_									
	T	T	G	v	Н	s	E	V	Q	L	Q	Q	S	G	P	E	L	E	K	P
181	ACT	ACA	GGT	GTC	CAC	TCT	GAG	GTC	CAG	CTG	CAG	CAG	TCT	GGA	CCT	GAG	CTG	GAG	AAG	CCT
	TGA	TGT	CCA	CAG			CTC		GTC	GAC		GTC	AGA	CCT	GGA	CTC	GAC	CTC	TTC	GGA
	G	Α	S	V	K	L	S	С	K	Α	S	G	Y	S	F	T	G	Y	N	M
241																			AAC	ATG
					TTC													ATG	TTG	TAC
	N	W	V	K	Q	S	H	G	K	S	L	E	W	I	G	H	I	D	P	Y
301					CAG			GGA								CAT			CÇT	
					GTC														GGA	
	Y	G	D	T	S	Y	N	Q	K	F	R	G	K	Α	T	L	T	٧	D	K
361																			GAC	
					AGG															
	S	S	S	T	A	Y	M	Q	L	K	S	L	T	S	E	D	S	A	V	Υ
421																			GTC	
																			CAG	
407	Y	C	V	K	G	G	Y	Y	G	H	W	Y	F	D	V	W	G	A	G	T
481																			GGG	
				TIC	CCC	CCA	ATG	AIG	CCC	GTG	ACC	AIG	AAG	CTA	CAG	ACC	CCG	CGT	CCC	TGG
		stEII	L - ~ ~ ~ -																	
	T	v	т	v	s	s	Α	т	т	т	A	P	s	v	Y	P	L	v	P	
541	-	•	-	•		_		_	-			_	_		_	_	_		CCG	GGC
3-11																			GGC	
	Baml			00	700	7.01	EcoF		101	101	-	001	HOA	CAG	AIA	000	AAC	Xhc		CCG
		. ~ ~ ~ .					~~~~~~											~~~	, <del>.</del>	
601	GGA	TCC	CCC	GGG	CTG	CAG	GAA	TTC	GAT	ATC	AAG	CTT	ATC	GAT	ACC	GTC	GAC	CTC	GAG	GGG
														_					CTC	
		-																		

The RACE product 3G4-2BVH is cloned and grafted onto the human  $\gamma 1$  constant region at the BstEII site. Thus, it contains the mouse leader sequence and its VH is joined with the human CH1 sequence in the following way: leader/3G4VH/VSS-AST...

	Mouse Leader	<b>↓</b> 1	mature protein		
1	MGWTWIFILI	LSVTTGVHSE	VQLQQSGPEL	EKPGASVKLS	CKASGYSFTG
51	YNMNWVKQSH	GKSLEWIGHI	DPYYGDTSYN	QKFRGKATLT	VDKSSSTAYM
				↓BstEII	graft site
101	QLKSLTSEDS	${\tt AVYYCVKGGY}$	YGHWYFDVWG	AGTTVTVSS A	ASTKGPSVFPL
151	APSSKSTSG			•	human viCH1

### FIG. 18B

### 3G4-2BVL original sequence:

																M	D	М	R	A
61																ATG	GAC	ATG	AGG	GCT
																TAC	CTG	TAC	TCC	CGA
	P	A	Q	I	L	G	F	L	L	L	L	F	P	G	T	R	С	D	I	Q
121	CCT	GCA	CAG	ATT	TTG	GGC	TTC	TTG	TTG	CTC	TTG	TTT	CCA	GGT	ACC	AGA	TGT	GAC	ATC	CAG
	GGA	CGT	GTC	TAA	AAC	CCG	AAG	AAC	AAC	GAG	AAC	AAA	GGT	CÇA	TGG	TCT	ACA	CTG	TAG	GTC
	M	T	Q	S	P	S	s	L	S	Α	S	L	G	Е	R	V	s	L	Т	C
181	ATG	ACC	CAG	TCT	CCA	TCC	TCC	TTA	TCT	GCC	TCT	CTG	GGA	GAA	AGA	GTC	AGT	CTC	ACT	TGT
	TAC	TGG	GTC	AGA	GGT	AGG	AGG	AAT	AGA	CGG	AGA	GAC	CCT	CTT	TCT	CAG	TCA	GAG	TGA	ACA
	R	Α	s	Q	D	I	G	S	s	L	N	W	L	Q	Q	G	P	D	G	T
241	CGG	GCA	AGT	CAG	GAC	ATT	GGT	AGT	AGC	TTA	AAC	TGG	CTT	CAG	CAG	GGA	CCA	GAT	GGA	ACT
	GCC	CGT	TCA	GTC	CTG	TAA	CCA	TCA			TTG	ACC	GAA	GTC	GTC	CCT	GGT	CTA	CCT	TGA
	I	K	R	L	I	Y	A	T	S	S	L	D	S	G	V	P	ĸ	R	F	s
301	ATT	AAA	CGC	CTG	ATC	TAC	GCC	ACA	TCC	AGT	TTA	GAT	TCT	GGT	GTC	CCC	AAA	AGG	TTC	AGT
	TAA	TTT	GCG	GAC	TAG	ATG	CGG	TGT		TCA	AAT	CTA	AGA	CCA	CAG	GGG	TTT	TCC	AAG	TCA
	G	s	R	S	G	s	D	Y	S	L	T	I	S	S	L	E	s	E	D	F
361																GAG			GAT	TTT
	CCG	TCA	TCC	AGA	CCC	AGT	ATD									CTC	AGA	CTT	CTA	
	V	D	Y	Y	С	L	Q	Y	V	S	S	P	P	T	F	G	A	G	T	K
421																GGT				
	CAT	CTG	ATA	ATG	ACA	GAT	GTT	ATA	CAA	TCA	AGA			TGC	AAG	CCA			TGG	TTC
												Bbs	sΙ				Ban	nΗΙ		
												~~~	~~~				~~~	-~	•	
	L	E	L	K	R	A	D	A	Α	P	T	V	F	I	F	G	R	I	P	
481					CGG											GGG				
	GAC	CTC	GAC	TTT	GCC	CGA	CTA	CGA	CGT	GGT	TGA	CAG	AAG	TAG	AAG	CCC	GCC	TAG	GGG	GCC

The RACE product 3G4-2BVL is grafted to human κ constant region at the BbsI site. Thus, it contains the mouse leader sequence and its VL is joined withIN the human CL1 sequence in the following way: leader/3G4-VL/TVF-IFP...

	Mouse L	eader	√mature pro	otein			
1	MDMRAPAQIL	GFLLLLFPGT	RCDIQMTQSP	SSLSASLGER	VSLTCRASQD		
51	IGSSLNWLQQ	GPDGTIKRLI	YATSSLDSGV	PKRFSGSRSG	SDYSLTISSL		
			FR4↓	↓Bb	sI graft site		
101	ESEDFVDYYC	LQYVSSPPTF	GAGTKLELKR	ADAAPTVF II	FPPSDEQLKSGTAS		
				↑	human kappa constant		

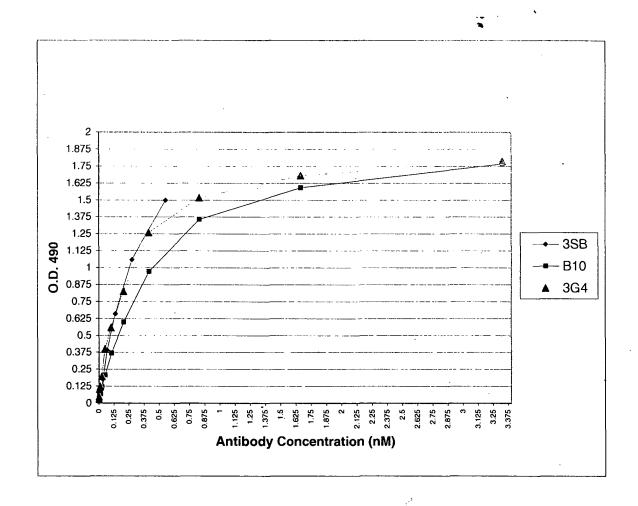


FIG. 19A

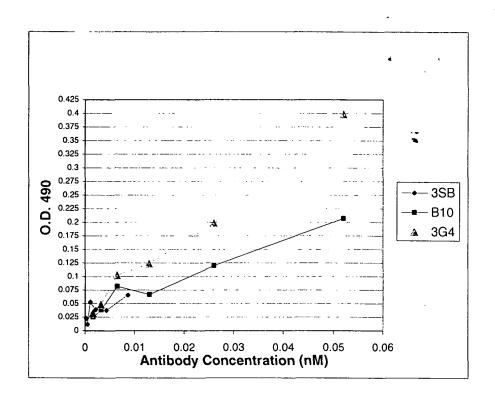


FIG. 19B

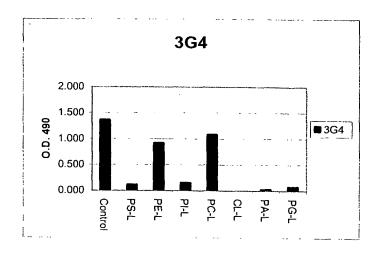


FIG. 20

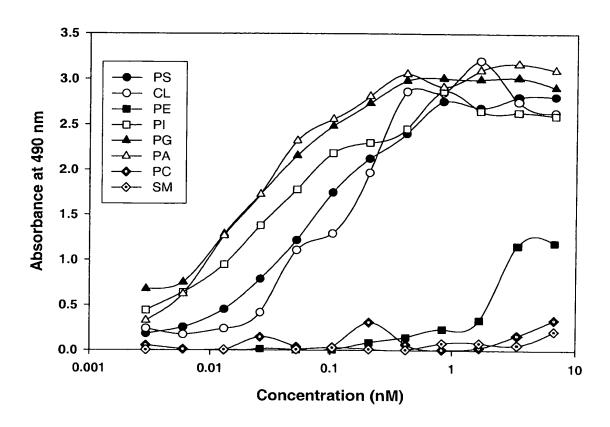


FIG. 21

LOCALIZATION OF CH3G4 TO BLOOD VESSELS IN

ORTHOTOPIC MDA-MB-435 TUMORS IN MICE

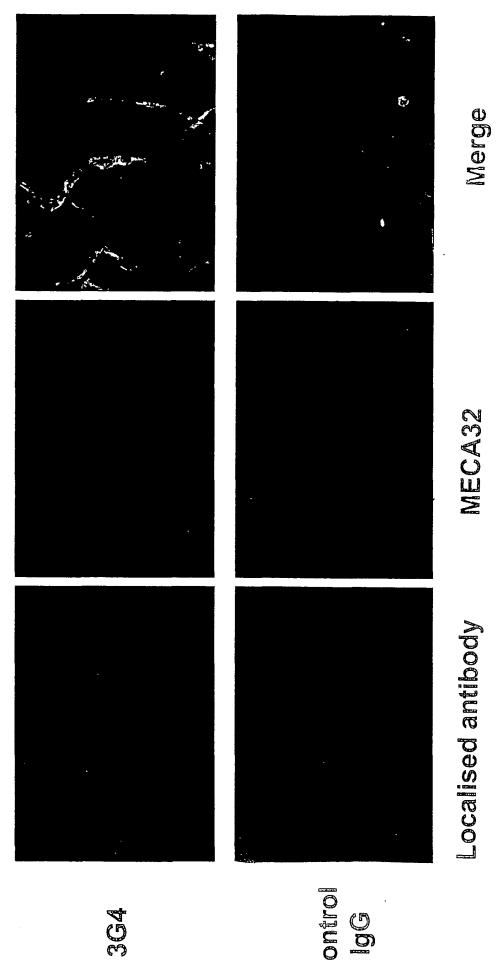
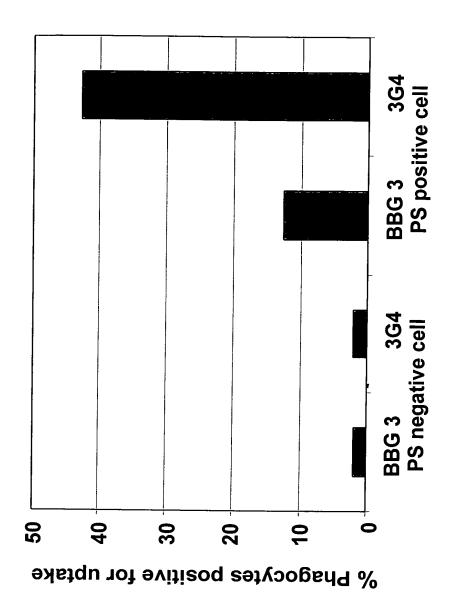
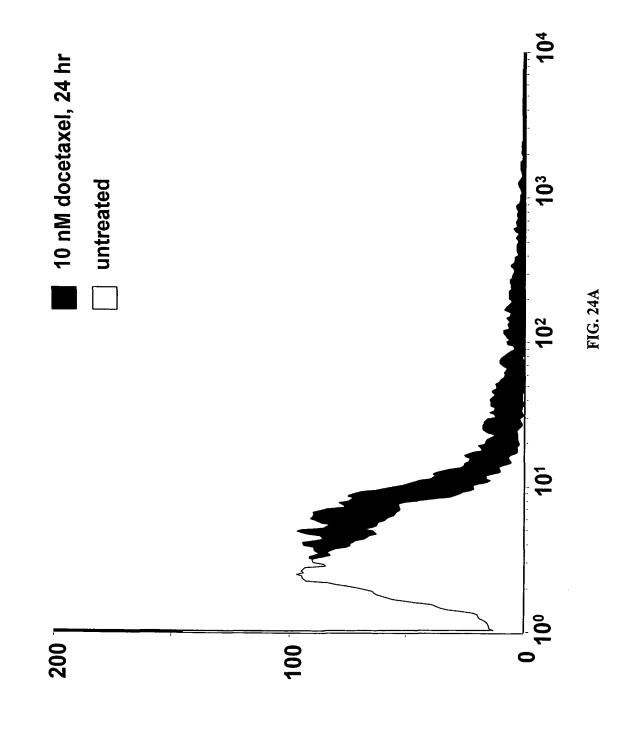


FIG. 22









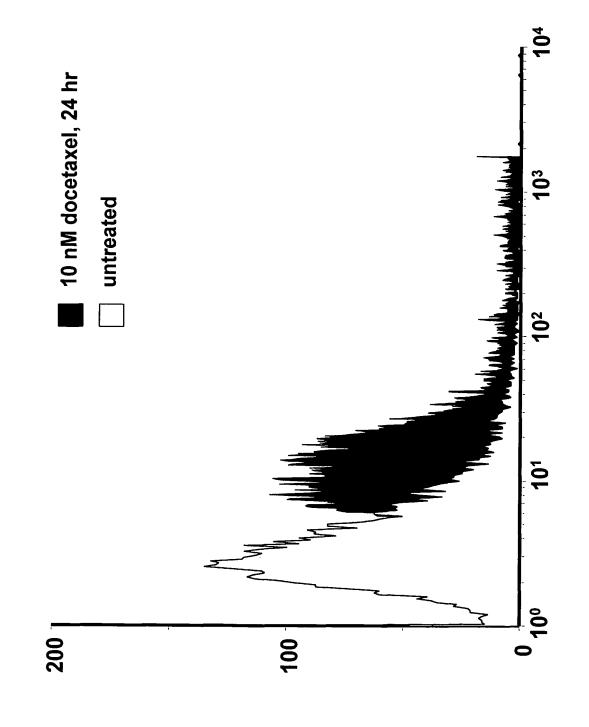
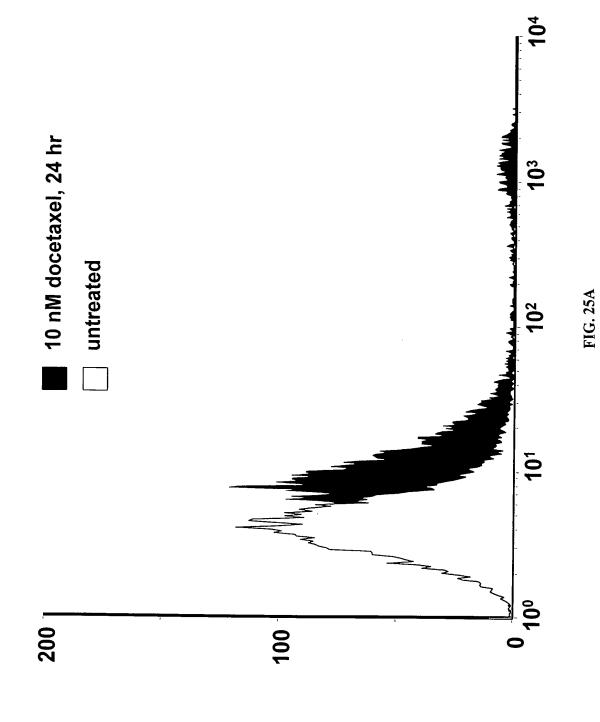
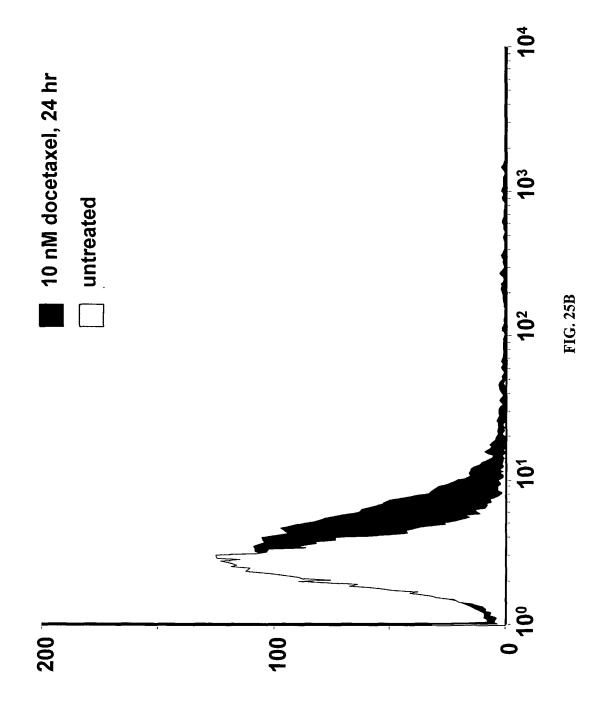
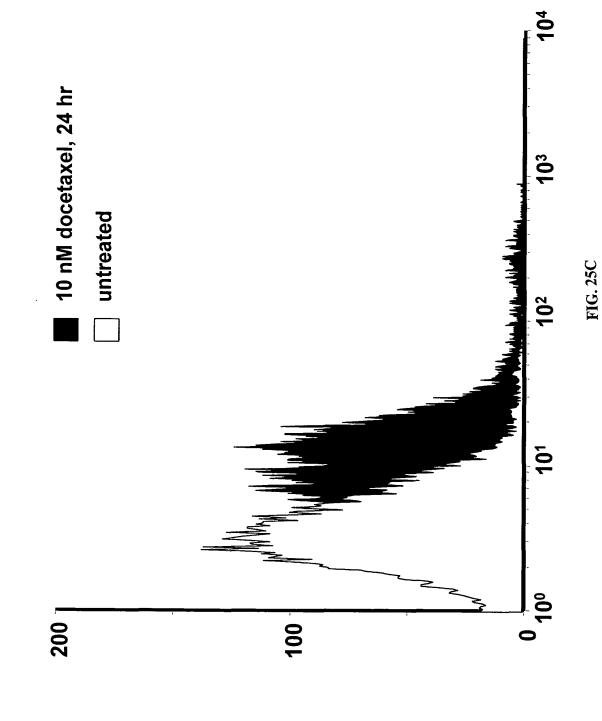


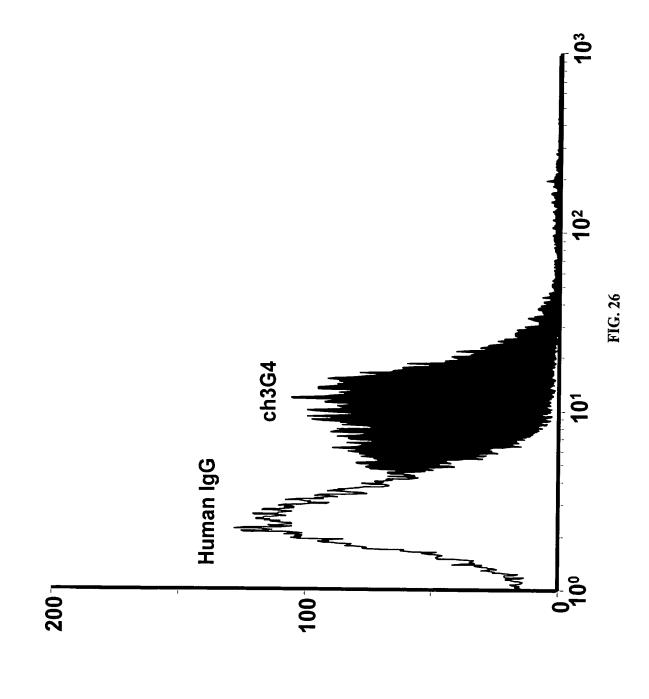
FIG. 24B





435s-luc





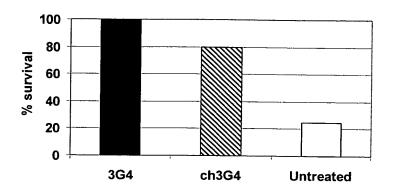


FIG. 27

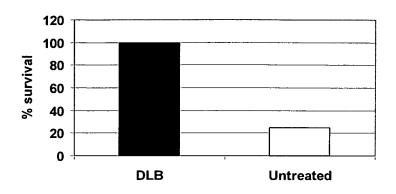
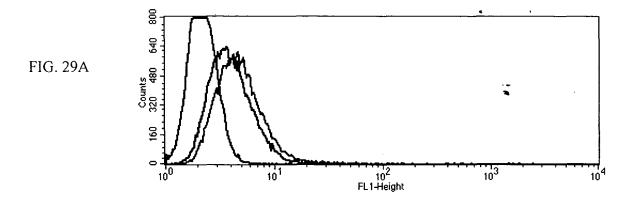
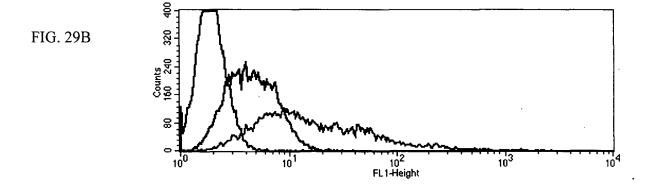
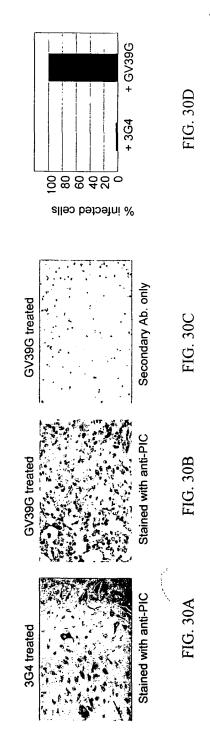


FIG. 28







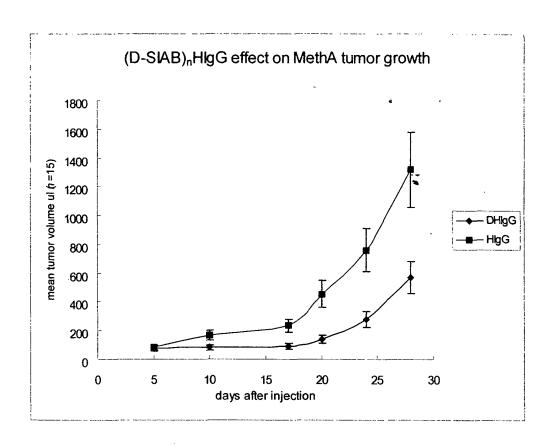


FIG. 31

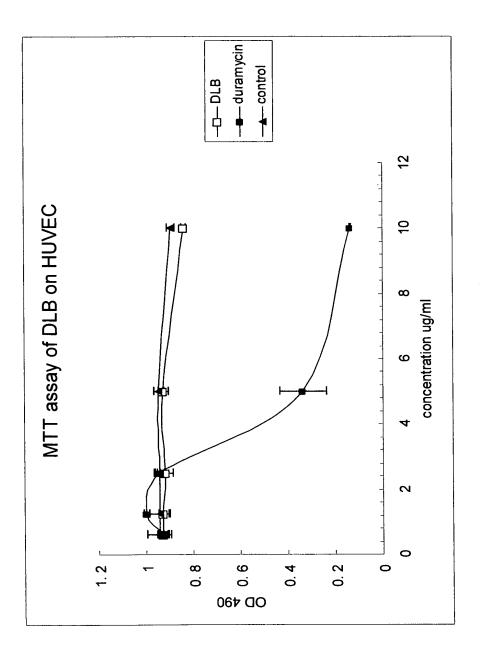


FIG. 32

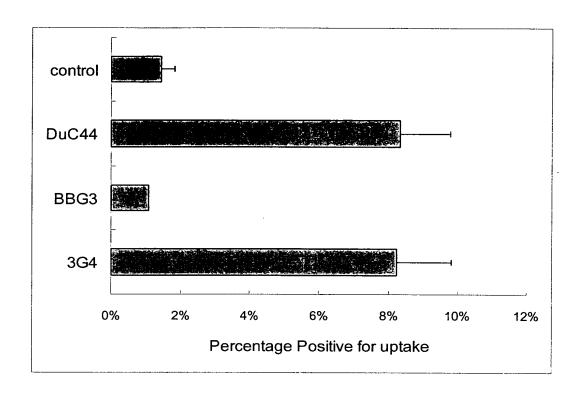


FIG. 33